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RAW SEQUENCE LISTING

DATE: 03/05/2003

PATENT APPLICATION: US/10/009,500B

TIME: 15:15:15

Input Set : A:\Merck233.app

Output Set: N:\CRF4\03052003\J009500B.raw

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3 <110> APPLICANT: KORDOWICZ, MARIA
4   GUESSOW, DETLET
5   HOFMANN, UWE
6   PACUSZKA, TADEUSZ
7   GARDAS, ANDRZEJ
9 <120> TITLE OF INVENTION: HYALURONIDASE FROM THE HIRUDINARIA MANILLENIS,
10  ISOLATION, PURIFICATION AND RECOMBINANT METHOD OF
11  PRODUCTION
13 <130> FILE REFERENCE: MERCK 2332
15 <140> CURRENT APPLICATION NUMBER: 10/009,500B
16 <141> CURRENT FILING DATE: 2002-04-08
18 <160> NUMBER OF SEQ ID NOS: 20
20 <170> SOFTWARE: PatentIn Ver. 2.1
22 <210> SEQ ID NO: 1
23 <211> LENGTH: 488
24 <212> TYPE: PRT
25 <213> ORGANISM: Hirudinaria manillensis
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32   20           25           30
34 Lys Gly Leu Trp Ser Phe Val Asp Ile Thr Ser Pro Lys Leu Phe Lys
35   35           40           45
37 Leu Leu Glu Gly Leu Ser Pro Gly Tyr Phe Arg Val Gly Gly Thr Phe
38   50           55           60
40 Ala Asn Trp Leu Phe Phe Asp Leu Asp Glu Asn Asn Lys Trp Lys Asp
41   65           70           75           80
43 Tyr Trp Ala Phe Lys Asp Lys Thr Pro Glu Thr Ala Thr Ile Thr Arg
44   85           90           95
46 Arg Trp Leu Phe Arg Lys Gln Asn Asn Leu Lys Lys Glu Thr Glu Asp
47   100          105          110
49 Asp Leu Val Lys Leu Thr Lys Gly Ser Lys Met Arg Leu Leu Phe Asp
50   115          120          125
52 Leu Asn Ala Glu Val Arg Thr Gly Tyr Glu Ile Gly Lys Lys Met Thr
53   130          135          140
55 Ser Thr Trp Asp Ser Ser Glu Ala Glu Lys Leu Phe Lys Tyr Cys Val
56 145          150          155          160
58 Ser Lys Gly Tyr Gly Asp Asn Ile Asp Trp Glu Leu Gly Asn Glu Pro
59   165          170          175
61 Asp His Thr Ser Ala His Asn Leu Thr Glu Lys Gln Val Gly Glu Asp
62   180          185          190
64 Phe Lys Ala Leu His Lys Val Leu Glu Lys Tyr Pro Thr Leu Asn Lys

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65          195          200          205
67 Gly Ser Leu Val Gly Pro Asp Val Gly Trp Met Gly Val Ser Tyr Val
68          210          215          220
70 Lys Gly Leu Ala Asp Gly Ala Gly Asp Leu Val Thr Ala Phe Thr Leu
71 225          230          235          240
73 His Gln Tyr Tyr Phe Asp Gly Asn Thr Ser Asp Val Ser Thr Tyr Leu
74          245          250          255
76 Asp Ala Thr Tyr Phe Lys Lys Leu Gln Gln Leu Phe Asp Lys Val Lys
77          260          265          270
79 Asp Val Leu Lys Asn Ser Gln His Lys Asp Lys Pro Leu Trp Leu Gly
80          275          280          285
82 Glu Thr Ser Ser Gly Tyr Asn Ser Gly Thr Lys Asp Val Ser Asp Arg
83          290          295          300
85 Tyr Val Ser Gly Phe Leu Thr Leu Asp Lys Leu Gly Leu Ser Ala Ala
86 305          310          315          320
88 Asn Asn Val Lys Val Val Ile Arg Gln Thr Ile Tyr Asn Gly Tyr Tyr
89          325          330          335
91 Gly Leu Leu Asp Lys Asn Thr Leu Glu Pro Asn Pro Asp Tyr Trp Leu
92          340          345          350
94 Met His Val His Asn Ser Leu Val Gly Asn Thr Val Phe Lys Val Asp
95          355          360          365
97 Val Ser Asp Pro Thr Asn Lys Ala Arg Val Tyr Ala Gln Cys Thr Lys
98          370          375          380
100 Thr Asn Ser Lys His Thr Gln Ser Arg Tyr Tyr Lys Gly Ser Leu Thr
101 385          390          395          400
103 Ile Phe Ala Leu Asn Val Gly Asp Glu Asp Val Thr Leu Lys Ile Asp
104          405          410          415
106 Gln Tyr Gly Gly Lys Lys Ile Tyr Ser Tyr Ile Leu Thr Pro Glu Gly
107          420          425          430
109 Gly Gln Leu Thr Ser Gln Lys Val Leu Leu Asn Gly Lys Glu Leu Lys
110          435          440          445
112 Leu Val Ser Asp Gln Leu Pro Glu Leu Asn Ala Asn Glu Ser Lys Thr
113          450          455          460
115 Ser Phe Thr Leu Ser Pro Lys Thr Phe Gly Phe Phe Val Val Ser Asp
116 465          470          475          480
118 Ala Asn Val Glu Ala Cys Lys Lys
119          485
122 <210> SEQ ID NO: 2
123 <211> LENGTH: 1464
124 <212> TYPE: DNA
125 <213> ORGANISM: Hirudinaria manillensis
127 <220> FEATURE:
128 <221> NAME/KEY: CDS
129 <222> LOCATION: (1)..(1464)
131 <220> FEATURE:
132 <221> NAME/KEY: variation
133 <222> LOCATION: (667)..(669)
134 <223> OTHER INFORMATION: This codon codes for a Tyr or Asn
136 <400> SEQUENCE: 2

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137 aaa gag att gcc gtg aca att gac gat aag aat gtg att gca tct gcc 48
138 Lys Glu Ile Ala Val Thr Ile Asp Asp Lys Asn Val Ile Ala Ser Ala
139 1 5 10 15
141 agt ggg tct ttc ctt gga gtt gcc ttt gat gcg tct cta ttt tcg ccc 96
142 Ser Gly Ser Phe Leu Gly Val Ala Phe Asp Ala Ser Leu Phe Ser Pro
143 20 25 30
145 aag ggt ctt tgg agc ttt gtt gat att acc tct cca aaa ttg ttc aaa 144
146 Lys Gly Leu Trp Ser Phe Val Asp Ile Thr Ser Pro Lys Leu Phe Lys
147 35 40 45
149 ttg ctg gaa gga ctt tct cct gga tac ttc agg gtt ggc gga acg ttt 192
150 Leu Leu Glu Gly Leu Ser Pro Gly Tyr Phe Arg Val Gly Gly Thr Phe
151 50 55 60
153 gcc aat tgg ctg ttt ttt gac ttg gac gaa aat aat aag tgg aag gat 240
154 Ala Asn Trp Leu Phe Phe Asp Leu Asp Glu Asn Asn Lys Trp Lys Asp
155 65 70 75 80
157 tat tgg gct ttt aaa gac aaa acc ccc gaa act gcg aca ata aca agg 288
158 Tyr Trp Ala Phe Lys Asp Lys Thr Pro Glu Thr Ala Thr Ile Thr Arg
159 85 90 95
161 aga tgg ctg ttc aga aaa caa aat aat ctg aaa aag gag act ttt gac 336
162 Arg Trp Leu Phe Arg Lys Gln Asn Asn Leu Lys Lys Glu Thr Phe Asp
163 100 105 110
165 aat tta gtg tta aaa cta aca aag gga agc aag atg aga ttg tta ttc gat 384
166 Asn Leu Val Lys Leu Thr Lys Gly Ser Lys Met Arg Leu Leu Phe Asp
167 115 120 125
169 ttg aat gcc gaa gtg agg act ggt tat gaa att gga aag aag atg aca 432
170 Leu Asn Ala Glu Val Arg Thr Gly Tyr Glu Ile Gly Lys Lys Met Thr
171 130 135 140
173 tcc act tgg gat tca tcg gag gct gaa aag tta ttt aaa tat tgt gtg 480
174 Ser Thr Trp Asp Ser Ser Glu Ala Glu Lys Leu Phe Lys Tyr Cys Val
175 145 150 155 160
177 tca aaa ggt tac gga gac aat atc gat tgg gaa ctt gga aat gaa ccg 528
178 Ser Lys Gly Tyr Gly Asp Asn Ile Asp Trp Glu Leu Gly Asn Glu Pro
179 165 170 175
181 gac cac acc tca gct cac aat tta act gaa aag cag gtt gga gaa gat 576
182 Asp His Thr Ser Ala His Asn Leu Thr Glu Lys Gln Val Gly Glu Asp
183 180 185 190
185 ttt aaa gca ctg cat aaa gtt cta gag aaa tat cca act ctt aac aag 624
186 Phe Lys Ala Leu His Lys Val Leu Glu Lys Tyr Pro Thr Leu Asn Lys
187 195 200 205
189 gga tcg ctc gtt ggt cca gat gta ggg tgg atg ggc gtc agt wac gtc 672
W--> 190 Gly Ser Leu Val Gly Pro Asp Val Gly Trp Met Gly Val Ser Xaa Val
191 210 215 220
193 aag gga ttg gca gac gag gcr ggt gac cat gta ack gct ttt aca ctc 720
194 Lys Gly Leu Ala Asp Glu Ala Gly Asp His Val Thr Ala Phe Thr Leu
195 225 230 235 240
197 cac caa tat tat ttc gat gga aac acy tct gat gta tca ata tat ctt 768
198 His Gln Tyr Tyr Phe Asp Gly Asn Thr Ser Asp Val Ser Ile Tyr Leu
199 245 250 255
201 gat gcc aca tac ttt aag aag ctg caa caa cta ttt gat aaa gtg aaa 816

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202 Asp Ala Thr Tyr Phe Lys Lys Leu Gln Gln Leu Phe Asp Lys Val Lys
203      260      265      270
205 gat gtt ttg aaa gat tct cca cat aaa gac gaa cca tta tgg ctt gga 864
206 Asp Val Leu Lys Asp Ser Pro His Lys Asp Glu Pro Leu Trp Leu Gly
207      275      280      285
209 gaa aca agt tct gga tac aac agc ggc aca gaa gat gta tcc gat cga 912
210 Glu Thr Ser Ser Gly Tyr Asn Ser Gly Thr Glu Asp Val Ser Asp Arg
211      290      295      300
213 tat gtt tca gga ttt cta aca tta gac aag ttg ggt ctc agt gca gcc 960
214 Tyr Val Ser Gly Phe Leu Thr Leu Asp Lys Leu Gly Leu Ser Ala Ala
215 305      310      315      320
217 aac aat gta aag gtt gtt ata aga cag aca ata tac aat gga tat tat 1008
218 Asn Asn Val Lys Val Val Ile Arg Gln Thr Ile Tyr Asn Gly Tyr Tyr
219      325      330      335
221 ggt ctc ctt gac aaa aac act tta gag ccg aat ccg gat tac tgg tta 1056
222 Gly Leu Leu Asp Lys Asn Thr Leu Glu Pro Asn Pro Asp Tyr Trp Leu
223      340      345      350
225 atg cat gtt cat aat tct ttg gtc gga aat aca gtt ttt aaa gtt gac 1104
226 Met His Val His Asn Ser Leu Val Gly Asn Thr Val Phe Lys Val Asp
227      355      360      365
229 gtt agt gat cca act aat aaa gca aga gtt tac gcg caa tgt acc aaa 1152
230 Val Ser Asp Pro Thr Asn Lys Ala Arg Val Tyr Ala Gln Cys Thr Lys
231      370      375      380
233 aca aat agc aaa cat act caa agc aga tat tac aag ggc tct ttg aca 1200
234 Thr Asn Ser Lys His Thr Gln Ser Arg Tyr Tyr Lys Gly Ser Leu Thr
235 385      390      395      400
237 atc ttt gca ctt aat gtt gga gat gga gat gta acg tta aag atc ggt 1248
238 Ile Phe Ala Leu Asn Val Gly Asp Gly Asp Val Thr Leu Lys Ile Gly
239      405      410      415
241 caa tac agc ggt aaa aaa att tat tca tac att ctg aca cct gaa gga 1296
242 Gln Tyr Ser Gly Lys Lys Ile Tyr Ser Tyr Ile Leu Thr Pro Glu Gly
243      420      425      430
245 gga caa ctt aca tca cag aaa gtt ctc ttg aat gga aag gaa ttg aac 1344
246 Gly Gln Leu Thr Ser Gln Lys Val Leu Leu Asn Gly Lys Glu Leu Asn
247      435      440      445
249 tta gtg tct gat cag tta cca gaa cta aat gca gat gaa tcc aaa aca 1392
250 Leu Val Ser Asp Gln Leu Pro Glu Leu Asn Ala Asp Glu Ser Lys Thr
251      450      455      460
253 tct ttc acc tta tcc cca aag aca ttt ggt ttt ttt gtt gtt tcc gat 1440
254 Ser Phe Thr Leu Ser Pro Lys Thr Phe Gly Phe Phe Val Val Ser Asp
255 465      470      475      480
257 gct aat gtt gaa gca tgy aar aar 1464
258 Ala Asn Val Glu Ala Cys Lys Lys
259      485
262 <210> SEQ ID NO: 3
263 <211> LENGTH: 488
264 <212> TYPE: PRT
265 <213> ORGANISM: Hirudinaria manillensis
267 <220> FEATURE:

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RAW SEQUENCE LISTING

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Output Set: N:\CRF4\03052003\J009500B.raw

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268 <221> NAME/KEY: variation
269 <222> LOCATION: (223)
270 <223> OTHER INFORMATION: Tyr or Asn
272 <400> SEQUENCE: 3
273 Lys Glu Ile Ala Val Thr Ile Asp Asp Lys Asn Val Ile Ala Ser Ala
274   1           5           10           15
276 Ser Gly Ser Phe Leu Gly Val Ala Phe Asp Ala Ser Leu Phe Ser Pro
277           20           25           30
279 Lys Gly Leu Trp Ser Phe Val Asp Ile Thr Ser Pro Lys Leu Phe Lys
280           35           40           45
282 Leu Leu Glu Gly Leu Ser Pro Gly Tyr Phe Arg Val Gly Gly Thr Phe
283           50           55           60
285 Ala Asn Trp Leu Phe Phe Asp Leu Asp Glu Asn Asn Lys Trp Lys Asp
286           65           70           75           80
288 Tyr Trp Ala Phe Lys Asp Lys Thr Pro Glu Thr Ala Thr Ile Thr Arg
289           85           90           95
291 Arg Trp Leu Phe Arg Lys Gln Asn Asn Leu Lys Lys Glu Thr Phe Asp
292           100          105          110
294 Asn Leu Val Lys Leu Thr Lys Gly Ser Lys Met Arg Leu Leu Phe Asp
295           115          120          125
297 Leu Asn Ala Glu Val Arg Thr Gly Tyr Glu Ile Gly Lys Lys Met Thr
298           130          135          140
300 Ser Thr Trp Asp Ser Ser Glu Ala Glu Lys Leu Phe Lys Tyr Cys Val
301           145          150          155          160
303 Ser Lys Gly Tyr Gly Asp Asn Ile Asp Trp Glu Leu Gly Asn Glu Pro
304           165          170          175
306 Asp His Thr Ser Ala His Asn Leu Thr Glu Lys Gln Val Gly Glu Asp
307           180          185          190
309 Phe Lys Ala Leu His Lys Val Leu Glu Lys Tyr Pro Thr Leu Asn Lys
310           195          200          205
W--> 312 Gly Ser Leu Val Gly Pro Asp Val Gly Trp Met Gly Val Ser Xaa Val
313           210          215          220
315 Lys Gly Leu Ala Asp Glu Ala Gly Asp His Val Thr Ala Phe Thr Leu
316           225          230          235          240
318 His Gln Tyr Tyr Phe Asp Gly Asn Thr Ser Asp Val Ser Ile Tyr Leu
319           245          250          255
321 Asp Ala Thr Tyr Phe Lys Lys Leu Gln Gln Leu Phe Asp Lys Val Lys
322           260          265          270
324 Asp Val Leu Lys Asp Ser Pro His Lys Asp Glu Pro Leu Trp Leu Gly
325           275          280          285
327 Glu Thr Ser Ser Gly Tyr Asn Ser Gly Thr Glu Asp Val Ser Asp Arg
328           290          295          300
330 Tyr Val Ser Gly Phe Leu Thr Leu Asp Lys Leu Gly Leu Ser Ala Ala
331           305          310          315          320
333 Asn Asn Val Lys Val Val Ile Arg Gln Thr Ile Tyr Asn Gly Tyr Tyr
334           325          330          335
336 Gly Leu Leu Asp Lys Asn Thr Leu Glu Pro Asn Pro Asp Tyr Trp Leu
337           340          345          350
339 Met His Val His Asn Ser Leu Val Gly Asn Thr Val Phe Lys Val Asp

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RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: US/10/009,500B

DATE: 03/05/2003
TIME: 15:15:16

Input Set : A:\Merck233.app
Output Set: N:\CRF4\03052003\J009500B.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:2; Xaa Pos. 223

Seq#:3; Xaa Pos. 223

VERIFICATION SUMMARY

DATE: 03/05/2003

PATENT APPLICATION: US/10/009,500B

TIME: 15:15:16

Input Set : A:\Merck233.app

Output Set: N:\CRF4\03052003\J009500B.raw

L:190 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:672

L:312 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:208